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Research Paper

Electrical neuromodulation of the cervical spinal cord facilitates forelimb skilled function recovery in spinal cord injured rats

Monzurul Alam [a,1], Guillermo Garcia-Alias [a,1], Benita Jin [a], Jonathan Keyes [a], Hui Zhong [a], Roland R. Roy [a,b], Yury Gerasimenko [a,c,d], Daniel C. Lu [e], V. Reggie Edgerton [a,b,f,g,*]

[a] Department of Integrative Biology and Physiology, University of California, Los Angeles, CA 90095, United States
[b] Brain Research Institute, University of California, Los Angeles, CA 90095, United States
[c] Pavlov Institute of Physiology, St. Petersburg 199034, Russia
[d] Institute of Fundamental Medicine and Biology, Kazan Federal University, Kazan 420006, Russia
[e] Departments of Neurosurgery, University of California, Los Angeles, CA 90095, United States
[f] Departments of Neurobiology, University of California, Los Angeles, CA 90095, United States
[g] Departments of Neuroscience, University of California, Los Angeles, CA 90095, United States

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ABSTRACT

Enabling motor control by epidural electrical stimulation of the spinal cord is a promising therapeutic technique for the recovery of motor function after a spinal cord injury (SCI). Although epidural electrical stimulation has resulted in improvement in hindlimb motor function, it is unknown whether it has any therapeutic benefit for improving forelimb fine motor function after a cervical SCI. We tested whether trains of pulses delivered at spinal cord segments C6 and C8 would facilitate the recovery of forelimb fine motor control after a cervical SCI in rats. Rats were trained to reach and grasp sugar pellets. Immediately after a dorsal funiculus crush at C4, the rats showed significant deficits in forelimb fine motor control. The rats were tested to reach and grasp with and without cervical epidural stimulation for 10 weeks post-injury. To determine the best stimulation parameters to activate the cervical spinal networks involved in forelimb motor function, monopolar and bipolar currents were delivered at varying frequencies (20, 40, and 60 Hz) concomitant with the reaching and grasping task. We found that cervical epidural stimulation increased reaching and grasping success rates compared to the no stimulation condition. Bipolar stimulation (C6– C8 + and C6 + C8–) produced the largest spinal motor-evoked potentials (sMEPs) and resulted in higher reaching and grasping success rates compared with monopolar stimulation (C6– Ref + and C8– Ref +). Forelimb performance was similar when tested at stimulation frequencies of 20, 40, and 60 Hz. We also found that the EMG activity in most forelimb muscles as well as the co-activation between flexor and extensor muscles increased post-injury. With epidural stimulation, however, this trend was reversed indicating that cervical epidural spinal cord stimulation has therapeutic potential for rehabilitation after a cervical SCI.

1. Introduction

Electrical stimulation of the spinal cord is a promising therapy for the rehabilitation of sensorimotor function after a spinal cord injury (SCI) (Edgerton and Roy, 2012; Jackson and Zimmermann, 2012; Dietz and Fouad, 2014; Alam et al., 2016). Stimulation of the lumbosacral spinal cord has resulted in successful restoration of weight-bearing standing and stepping in complete paraplegic cats and rats (Gerasimenko et al., 2003; Saigal et al., 2004; Ichiyama et al., 2005; Gerasimenko et al., 2007; Courtine et al., 2009; Musienko et al., 2009; Wenger et al., 2014). Spinal cord stimulation at the lumbosacral cord in human subjects with a clinically complete SCI has resulted in recovery of standing and of some volitional control of leg movements as well as improvement in autonomic function (Minassian et al., 2004; Harkema et al., 2011; Angeli et al., 2014).

Restoration of arm and hand function is one of the highest priorities of individuals with a cervical SCI (Anderson, 2004). Previous work has shown that intraspinal stimulation at the cervical segments of the spinal cord elicits motor responses in multiple forelimb muscles in rats (Sunshine et al., 2013) and that selected stimulation parameters can facilitate functional reaching and grasping movements in non-injured monkeys (Zimmermann et al., 2011; Sharpe and Jackson, 2014). It also has been shown that chronic intraspinal stimulation at the cervical spinal cord can improve forelimb function in rats with a cervical SCI

* Corresponding author at: Department of Integrative Biology and Physiology, University of California, Los Angeles, 610 Charles E. Young Drive, Los Angeles, CA 90095-1527, United States.
E-mail address: vre@ucla.edu (V.R. Edgerton).
[1] MA and GGA contributed equally to this work.

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